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UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

DREW SCIENTIFIC, INC., Plaintiff, -v- POINTCARE TECHNOLOGIES, INC., Defendant.	08 CV 1490 (AKH) **REPLY DECLARATION OF GEORGE CHAPPELL IN FURTHER SUPPORT OF MOTION FOR PRELIMINARY INJUNCTION**

STATE OF TEXAS)
ss:
COUNTY OF DALLAS)

GEORGE CHAPPELL deposes and says:

1. I am employed by Drew Scientific, Inc. ("Drew") as its Chief Engineer. I respectfully submit this reply declaration in response to certain allegations asserted by PointCare Technologies, Inc. ("PointCare") in opposition to Drew's motion for a preliminary injunction. Specifically, the purpose of this declaration is to correct the more significant of the numerous misstatements in the affidavits of PointCare's Dr. Peter Hansen and Don Barry, Jr. To avoid burdening the Court, I have not tried to correct all such misrepresentations, but only those that I understand to be directly relevant to the dispute at hand.

POINTCARE'S SINGLE-DOSE "AuRICA" MACHINE WAS NOT A USEFUL MODEL FOR THE HT MACHINE

2. Perhaps the central misrepresentation that pervades both affidavits is that Drew's engineering task was simple, because PointCare had previously gotten its gold reagent to work in its AuRICA machine. Typical of this is Dr. Hansen's claim in paragraph 61 of his affidavit that: "We were not looking for new technology from Drew; a repeat of the AuRICA would be fine." Mr. Barry makes numerous similar statements as well.

3. Such statements are simply flat-out untrue. To understand why, the Court may wish to look at the AuRICA brochure on PointCare's web site. It lists Dr. Hansen as its author. (A true and correct copy of the brochure is annexed hereto as Exhibit A.) Dr. Hansen tells the Court that: "AuRICA already automatically performed the CD4Sure™ assay ...." What he does not tell the Court, however, is that it was only "automatic" for a single dose at a time. As Dr. Hansen admits on pages 7-8 of his brochure, after each and every dose the AuRICA test, the operator has to manually change two tubes – both the whole blood sample tube and also the tube containing the dried CD4 antibody reagent.

4. If all that PointCare was demanding of Drew was a machine in which tubes needed to be manually changed after every dose, we could have provided such a machine in no time. Indeed, our existing Excel 22 machine already had a direct-entry option. But that was not what PointCare wanted. <u>Indeed, they directed us to remove the direct-entry option from the Excell 22</u>. Rather, in the specifications they provided us, and incorporated into the Agreement, they demanded the HT be able to "operate for minimum of 1 hour or 30 samples unattended." (A true and correct copy of this specification page from the Agreement is annexed hereto as Exhibit B.) PointCare's AuRICA machine had no way of doing that.

5. Perhaps the best analogy I can think of is the difference between engineering a

single soda can (the AuRICA), with the soda already mixed inside, versus engineering a fountain soda machine (the HT), in which the syrup, carbonation and water are all entered separately, and are then mixed automatically every time the user hits the button for a particular soda. The latter, obviously, presents the much more significant engineering challenge.

6. Accordingly, Drew could not rely on the AuRICA; rather, it had to engineer a new 30-unit device that would work with PointCare's gold reagent. While PointCare now complains about our "poor engineering choices" (*see* Barry Aff. ¶ 3), the truth of the matter is that we consulted with PointCare on engineering decisions at every step along the way, and in each instance Dr. Hansen and Mr. Barry agreed with the recommendations we had made. Never did they suggest to us that we should instead use the AuRICA design (which they never even shared with us). Indeed, such a suggestion would have been contrary to PointCare's own specifications, given that, as noted above, the AuRICA was a single dose machine. PointCare also claims Drew was "one year past the final completion date set forth in the Agreement." (*See* Barry Aff. ¶ 3.) What they are not saying, however, is that the HT completion date was repeatedly <u>revised</u> by the parties, after signing of the Agreement, without ever an objection from PointCare. (Indeed, many of the revisions were attributable to PointCare's delays, especially with regard to the uncompleted software.) That is because, in an engineering project, the timetable serves the ends of the project, not vice-versa.

7. Notwithstanding the challenges, Drew succeeded in engineering a 30-unit (32-unit, actually) from scratch, extremely fast. As even Mr. Barry admitted in his deposition (*see* Barry Depo. p. 99, lns. 14-18), the buildup of PointCare's gold reagent on the internal surface of the HT device was the principal cause of the engineering delays, as it prevented the machine's optical sensors from working properly. We tried all types of material substitutes, suggested by

both ourselves and PointCare, and could never get the optical sensors to pierce the gold residue. I eventually discovered (a discovery for which Mr. Barry now incorrectly takes credit) that the only real solution was to use an ultrasonic sensor instead. With that change, the gold adherence problem was solved, but Drew devoted considerable time and effort to redesigning the machine to accommodate the new sensor. Thus, last November, we had completed a fully functioning machine, but for the software PointCare had failed to install.

8. In his affidavit, Mr. Barry makes several misstatements about the gold reagent problem which calls into question either his veracity or his engineering know-how. First, he claims that the reason for the gold buildup was because "material surfaces … were not properly cleaned and polished." (See Barry Aff. ¶ 7.) That is just not the case. To test Mr. Barry's theory, we tried not only all the substances he proposed, such as polypropylene, but even glass, one of the smoothest surfaces known to man. All experienced the same problem. The issue was not the smoothness of the surface, as we told Mr. Barry repeatedly.

9. In paragraph 9 of his affidavit, Mr. Barry states that: "The intended higher volume capability of the HT … had no bearing on the 'gold adherence problem' in the HT." That too is incorrect. Gold carries an ionic charge which caused the gold reagent to stick to internal surfaces of the machine (smooth or not), eventually building up to a point where it obstructed the optics. This was never a problem with the AuRICA because a new gold reagent sample is installed in the test tube after every use, a process which eliminates the charge. In the 32-dose HT machine, however, the gold's ionic charge remained. Hence, the problem.

10. Mr. Barry also claims that he warned us of the problem in June 2006. (*See* Barry Aff. ¶ 4, Ex. 1.) That is not quite accurate. Gary Young took notes of that meeting, which are annexed as Exhibit 1 to the Mr. Barry's affidavit. They reflect that Mr. Barry gave us the wrong

warning. First, the notes reflect that Mr. Barry told us the gold reagent would only buildup "after one month." In fact, it would build up on the first day of use. Second, the notes reflect that Mr. Barry told us the gold reagent would have "no effect on tygon or delrin," since the reaction time between the gold and the surface was too short to have a deleterious effect. Tygon is a flexible plastic tubing that is not useable for the internal surface of a hematology device. As for Delrin, we tested the material, and it did not work. Indeed, months later, Mr. Barry apologized to Drew for this incorrect advice, as I discuss below.

11. Not only was PointCare's advice worse than useless for solving the gold reagent buildup issue, but PointCare obstructed the engineering process in a myriad of different ways. I discuss these facts at greater length in my deposition, but for purposes of this affidavit I will highlight some of the biggest problems. Perhaps most importantly, Dr. Hansen and Mr. Barry rarely made himself available to Drew after the initial meetings, instead sending a relatively inexperienced junior employee, Amy Coughlin, to Drew's engineering facility in Texas to learn how the HT machine worked so that PointCare could service it. PointCare never completed the software they had promised us. PointCare never provided to us sufficient gold reagent to even test the prototype. (Contrary to Mr. Barry's affidavit, the only gold reagent they provided to us in 2006 was expired.) And they were reluctant to provide with their internal data, which we could have used as a benchmark for our testing.

12. But perhaps the most egregious statement in either affidavit is Mr. Barry's claim that the proposed HT project was a 'low risk' project." (*See* Barry Aff. ¶ 6.) I do not understand how Mr. Barry can possible reconcile this statement with his candid admission, in a March 16, 2007 email to Gary Young which was later shared with me, that: "This reagent is very difficult to deal with and we have been stumped and have had three or four other engineering groups

stumped at finding materials that can be machined and are compatible." (A true and correct copy of Mr. Barry's email is annexed hereto as Exhibit C.)

13. In short, the Drew engineering staff solved a problem that had "stumped" both PointCare and three to four other companies. We are proud of that achievement, and proud of the work we have done to develop the HT machine. Unfortunately, rather than congratulate us for our accomplishment, Messrs. Hansen and Barry now see fit to insult us for not solving the problem fast enough to their liking. The truth of the matter is that we have solved the problem, and last December advised PointCare that we had ready for delivery a functioning machine. To date, they have refused to accept delivery. Had they done so back in December, I believe that the machine would now be on the market.

Conclusion

14. For all of the reasons articulated herein, I respectfully submit this reply declaration in further support of Drew's motion for a preliminary injunction. I declare under penalty of perjury of the laws of the United States of America that the foregoing is true and correct to the best of my knowledge.

Dated: April 30, 2008

GEORGE CHAPPELL

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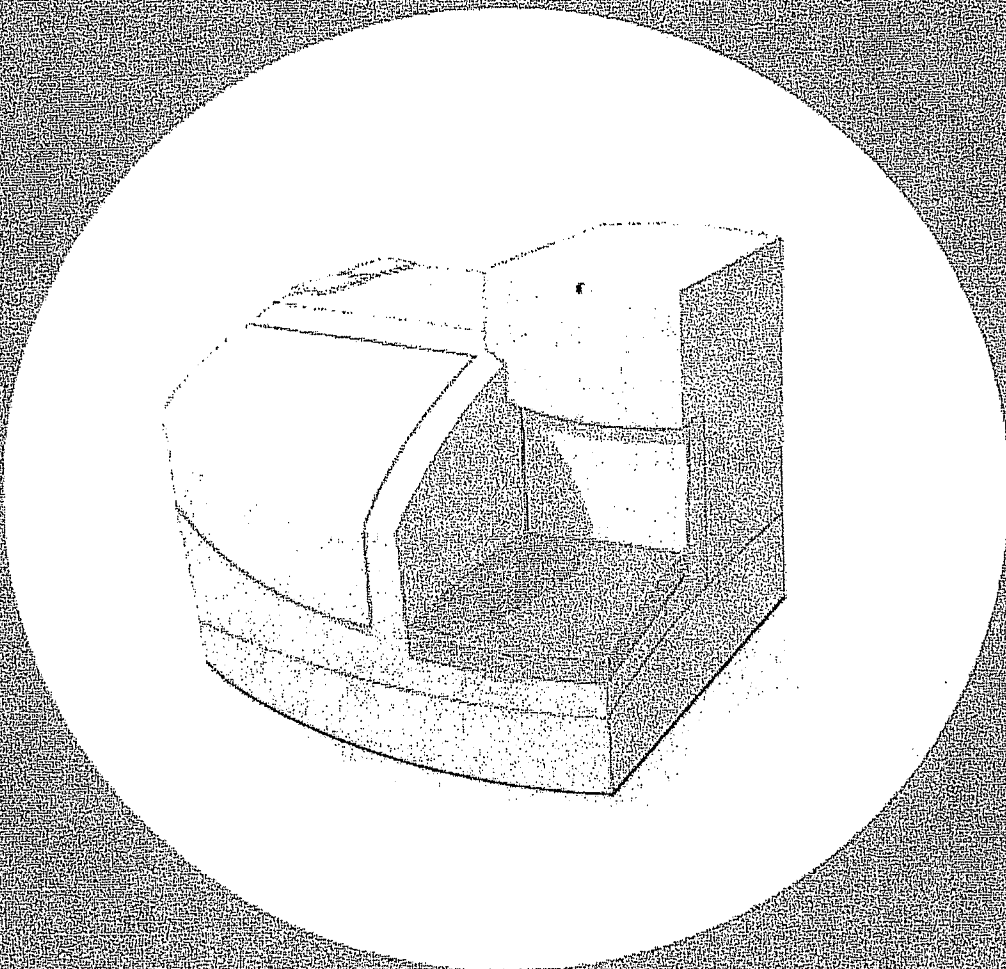
EXHIBIT A

PointCare Technologies Inc.

SYSTEM OVERVIEW

AuRICA

W. Peter Hansen, PhD.



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INTRODUCTION

The AuRICA instrument was developed only after a thorough study of the diagnostic monitoring requirements of worldwide Anti Retroviral therapy (ARV) programs. As such, AuRICA is an essential companion to ARV administration regimens that provide caregivers with numerical information concerning CD4 lymphocyte and absolute counts, and white cell counts for management of opportunistic infections.

In order to offer features that the study showed to be indispensable, it was necessary to eliminate traditional fluorescence-based CD4 counting and replace it with a novel, very robust, and low cost-of-manufacturing technology. Having done this, the single platform AuRICA system offers important features such as internal automated pipetting from sealed phlebotomy tubes, storage of reagents without refrigeration, automated cluster finding and counting, all results (including hematology) on the same run, results that do not require operator interpretation, automated internal quality control, automated start-up and shut-down, immunity to poor quality power, and portability. Finally, being highly automated and therefore simple-to-use, the system is an immediate companion to ARV programs even during the current, severe, worldwide shortage of trained diagnostic monitoring technicians.

The next section of this report provides more detail connecting the survey and the design of the AuRICA system, with special attention to design improvements incorporated from field evaluations.

DESIGN CRITERIA

Design Criteria with a Sociologic Basis

Worldwide ARV programs cannot be successful if the needs and rights of patients outside urban centers are not respected. These needs and rights are simple to enumerate.

After having established that a patient is HIV positive and during the years leading up to the time for ARV administration, that patient should ideally have a continuous record of several CD4 and other diagnostic tests per year. As the pandemic comes under better control, the number of years of testing, and hence the number of tests, will increase because patients will come to care sooner than is the case now. It is technically possible to bring diagnostic monitoring to the patient so that the patient can learn their status, receive advice and counsel, and return home or to work in a few hours time. Being technically possible, it becomes the patient's right to local care and not to be forced to travel excessively for ARV monitoring.

Trips to local clinics can be relatively inconspicuous and, as such, some of the stigma of HIV/AIDS can be avoided. Local clinics are frequently discretely situated allowing patients reasonable privacy. Repeated trips to a distant urban testing center are difficult to disguise.

Obtaining a result while the patient waits less than 15 minutes can be used to the advantage of the caregiver to lessen patient anxiety. Waiting days to inform a patient of their status, or frequently waiting months to inform them on their return for a follow-up test, is at best a lost opportunity to keep the patient "in the Program," and at worst cruel, bureaucratic torture. Obtaining a result while the patient is still present also simplifies logistics and with that comes reductions in cost.

Design Criteria with an Operational Basis

Accurate pipetting requires diligent training, but even with the best of training programs, it remains a problem. One simple reason is that trained staff are never permanent; therefore training becomes a costly and continuous activity. A second factor is that pipette calibration needs to be maintained and that can be cost prohibitive because the lab will need two sets of pipettes–one set for use while the other set is at the calibration facility.

Therefore, the first operational design criterion was that the AuRICA system would perform all fluid handling steps, and that the operator would need no

pipetting skills at all. All patient samples are potentially dangerous and training in the safe handling of open specimens is another costly and continuous program.

The second operational design criterion was that AuRICA should work without opening the sample tube, and that all waste be contained. The system should have an internal, cap-piercing pipette for this purpose.

Training technicians in the art of interpreting flow cytometry dot plots by visual inspection and using visual subjective means to control the quality of results is a luxury that may work well in some privileged venues, but it is not possible in the face of the worldwide shortage of trained operators.

The third operational design criterion was that AuRICA should have automatic cluster finding and internal quality control of the system. The internal quality control points should not only be cluster quality but also points such as flow rate profile monitoring, monitoring and maintaining minimum pipette probe depth in a sample, monitoring reaction temperatures, and monitoring and maintaining line power quality.

The fourth operational design criterion was that reagents be insensitive to light and be stable at elevated temperatures without the need for refrigeration, as it is not possible to refrigerate reagents or keep them in the dark at remote point of care sites. Achieving this required inventing a new detection technology for AuRICA, because this is not possible with today's fluorescence reagents.

The fifth design criterion was that AuRICA must be mechanically robust and require no more than 30 minutes for the operator to set up and take down, as remote care requires portable systems. The operator should need no special training for this, and the system should only need a control run after set-up to be ready for patient samples.

The sixth design criterion was that AuRICA must successfully lyse so-called "hard to lyse" samples and report accurate results.

Design Criteria with an Economic Basis
Cost is a paramount issue, particularly in the developing world. The AuRICA system was designed using an economic model that captures all costs (hidden and apparent) that are involved in reporting a patient result. These costs include: instrument cost, instrument service cost including special "service policies" for laser replacement, reagent costs, refrigerated reagent storage costs, training costs, labor costs, cost of associated supplies, waste disposal cost, and

the cost of control runs. Of these, training costs and instrument costs are the most significant. There is a worldwide shortage of trained technicians, and the immense cost of solving this problem can be contained if diagnostic instrumentation can be fully automated and operated by people with only an "ultra-short course" of training. There is no need for fully automated instrumentation to be expensive in the face of modern technology. Consequently, the economic design criteria for AuRICA were: Use up-to-date science and technology to create a new, fully automated system that can be run by almost anyone, at a small fraction of the cost that is normally associated with manufacturing fully automated diagnostic instruments. Pass this savings on to the user in the form of an affordable total cost to obtain a complete patient result.

Another aspect of cost savings concerns the logistics of samples, data and patients. Even when technologies are available that permit the analysis of samples that are a day old, the cost of reliable shipping must be considered. Additionally there is the cost of collating and exporting data back to the local clinic. Of course, there is the "hidden" cost of finding the patient and having the patient return to the clinic if the result requires action, or if the clinic wishes to simply reassure the patient.

The next section of this report describes the operation of the AuRICA system from the user's perspective. This description can be compared to the design criteria outlined above.

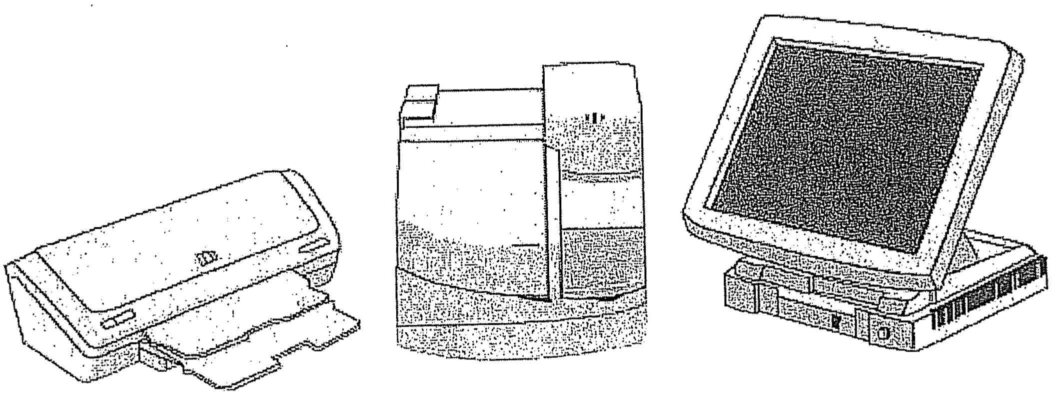
OPERATION OF THE AURICA SYSTEM

Unpacking and Initial Operation

The system arrives packed in a container that is not to be discarded, but should be stored and used in the event of subsequent air or ground shipment. There are four components, the printer, the touch screen computer, the instrument (shown in Figure 1) and the reagent kit. The recipient connects the electrical cable (USB cable) between the computer and instrument and connects the instrument to an electrical power source.

The system accepts all conventional alternating current (AC) power sources with 100v to 240v and 47 Hz to 63 Hz. An optional, uninterruptible power supply (UPS) would allow the system to operate over wider ranges of voltage and frequency in regions with poor quality power. The UPS maintains the input power under low voltage or high voltage variations, and allows the system to finish the sample it is currently processing and execute the automated shut down procedure from a battery back-up in the UPS if the power should fail completely.

Figure 1: The Hardware Components of the AuRICA System: the Printer, the Instrument, and the Touch Screen Computer

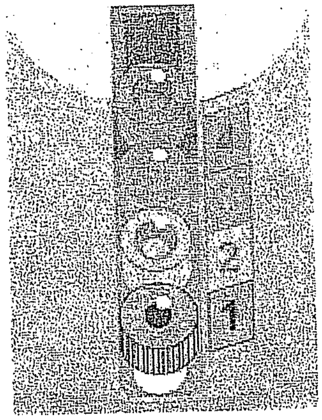


Principles of the Closed Tube Volumetric Sub-system

Figure 2 gives detail of the sample and reagent loading compartment, called the vial block. Four sealed tubes, 3 of which are supplied in the CD4 Reagent Kit, are placed in the vial block. All tubes are barcoded and read inside the instrument as a quality control check that each is in the correct position, that certain tubes are not being reused, as well as to check whether the tube has reached its expiration date. When analyzing patient samples, the tube in position 1 is the whole blood sample tube, such as K2 or K3 EDTA tubes including the Vacutainer™ tube, direct from the phlebotomist. The tube in position 2 contains

dried CD4 antibody reagent. Tubes 1 and 2 are changed with each patient sample. The tubes in positions 3 and 4 are for lysing and cleaning and are sufficient for 10 patient samples.

Figure 2: The Vial Block in Which Sample and Reagent Tubes Are Loaded For Analysis



After the tubes are loaded and the patient identification information is entered on the computer touch screen, the tube rack disappears inside the instrument and is not accessible by the operator. Then begins a computer controlled sequence of pipetting, mixing and incubation steps.

All pipetting steps are carried out by cap piercing probes and none are carried out by the operator. These have several special features. First, the probes are guided by an electronic liquid level sensor. This means that any volume of blood in the sample tube that is greater than 0.5 mL can be sampled accurately. The electronic probe guidance system is not susceptible to blood that may by retained under the cap of the phlebotomy tube. The probes have a self-aligning mechanism to target the center of the tube cap and maintain centering while in the tube. The probes are subjected to rigorous cleaning at all steps of the process. More than half of the AuRICA sample processing time is used for fluid component cleaning; from the cap-piercing probes to the flow cytometry flow cell. Carry-over data is shown in a later section of this report that attests to the efficacy of these cleaning steps.

Pipetting is driven by precision syringe pumps. All measurements in AuRICA are performed on absolute volumes of fluid dispensed and aspirated by these syringe pumps. For example, 25 μL of blood is aspirated and dispensed with a volumetric precision of 2.5%. All other pipetting steps are also precise to 2.5%. These pumps also drive the sample and sheath during the flow analysis phase of

the sample process. The sample flow rate is continuously monitored and checked during this phase as an internal quality control point.

Mixing is also carried out automatically inside the instrument, in the form of axial vortexing. A device rotates the tubes at controlled rates and at specific times also serves as the barcode reader. Training an operator in proper vortexing technique is therefore completely avoided.

The antibody incubation and the lysing steps are temperature controlled at 37° Celsius. There are no off-line incubations to be carried out by the operator. The system can operate in environments where the temperature is between 16° and 32° Celsius (60°F to 89°F) and from 10% to 80% non-condensing humidity.

The system has several automated, internal quality control features concerning maintenance. At the end of a normal day of operation the user loads a special shutdown tube into the tube rack, replaces the sheath with special shutdown solution, touches "Begin Shutdown" on the screen and leaves. The system spends the next 1.5 hours executing a daily clean cycle. No operator training is needed for shutdown. This procedure is also enforced when the machine has been idle for 8 or more hours if a shutdown procedure has not been completed.

If the instrument has not run a sample for two hours during the normal daily operation, then a thirty second cycle automatically starts and runs a small amount of fluid through the system into the waste container, thereby objectively checking the readiness of the system.

There is a special shutdown sequence to prepare the system for air shipment.

Principles of the Identification and Classification of Cells

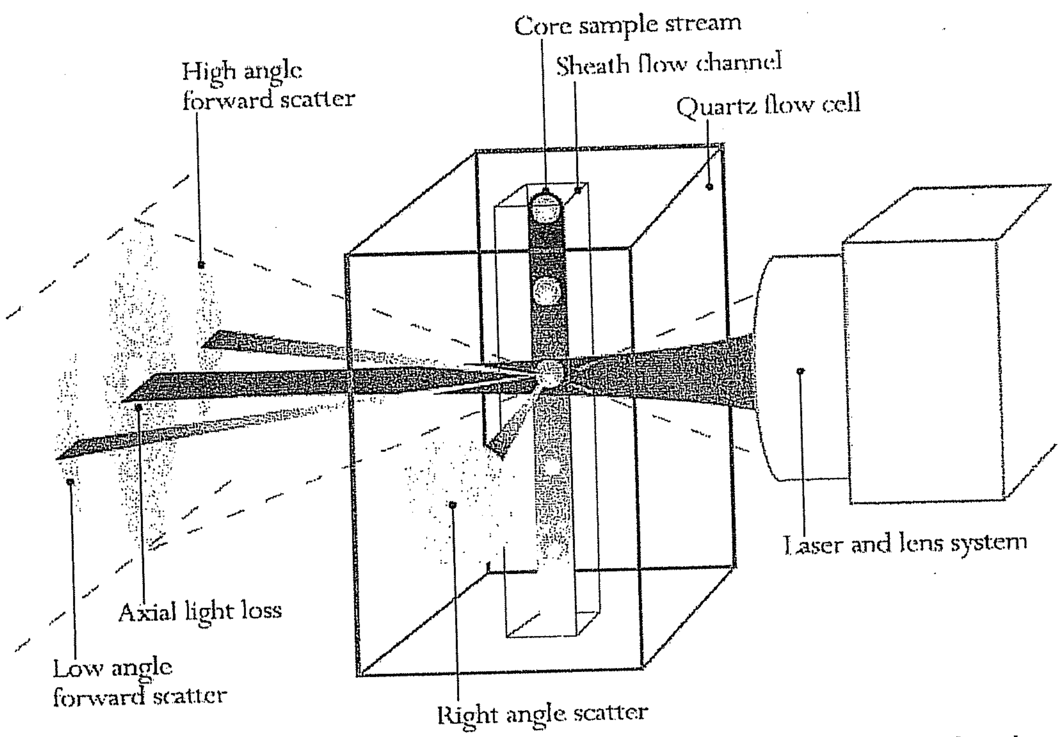
While the AuRICA system is a flow cytometer, it uses a new method for the identification, classification, and counting of cells that is based on the physics of light scatter and not on fluorescence. This new method is responsible for the low cost and mechanical stability of the system.

In conventional flow cytometry, combinations of multi-color fluorescence and light scatter are used to identify certain characteristics of cells. For example, one color may be used to identify a cell as being a white cell and another to identify the cell as a T lymphocyte, and when these are combined with right angle scatter it becomes possible to identify CD4 positive lymphocytes. In AuRICA, "colors of fluorescence" are eliminated and replaced by "angles of light scatter" as will be more fully described below.

AuRICA uses four light scatter detectors placed at three different angles. Each of these detectors has a different range of angles over which it accepts light. They are shown in Figure 3 and have the following light scatter acceptance angles:

Forward scatter low (FSL)	1° to 2°
Forward scatter high (FSH)	8° to 12°
Right angle scatter (RAS)	45° to 135°
Extinction (EXT)	0°

Figure 3: Exploded View of the Four Light Scatter Detectors Placed at Four Different Angles.



In practice the detectors are part of a microchip assembly that is rigidly mounted to the flow cell. Axial light loss provides an extinction signal (EXT) and a time of flight signal (TOF) that is used for lymphocytes and monocytes, high angle forward scatter (FSH) provides a granulocyte marker, and right angle scatter (RAS) has a backscatter component that provides a CD4 cell marker.

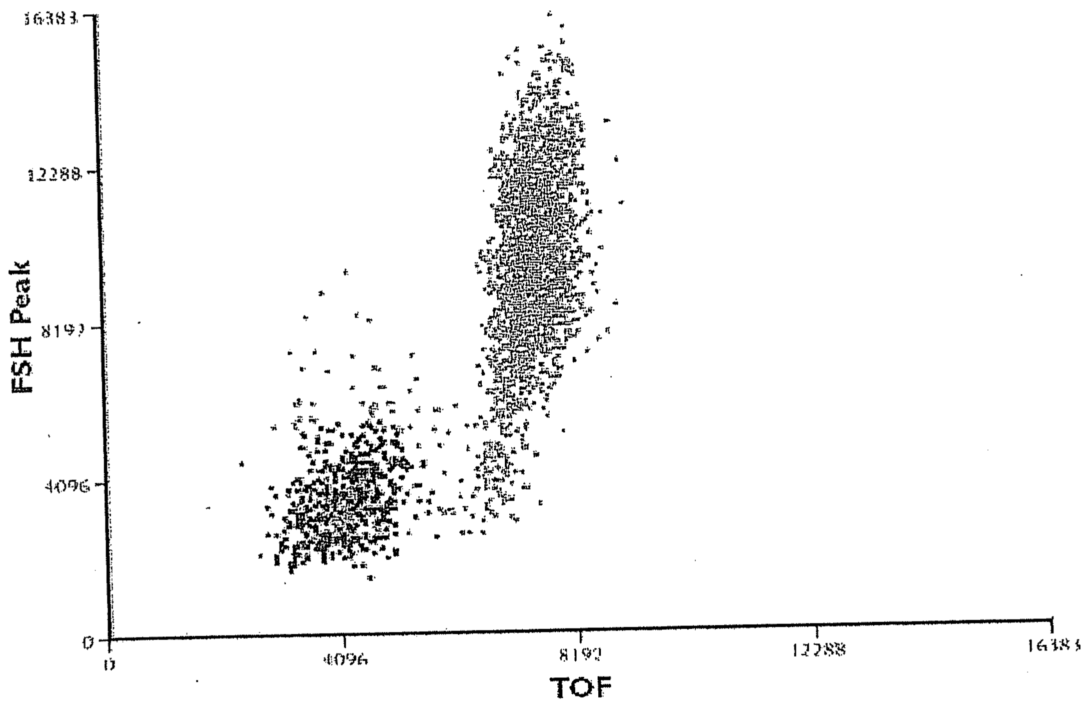
Each of these detectors is used to identify certain characteristics of cells. This can be best described as follows. Detectors placed at low angles of forward scatter (e.g. FSL) respond mostly to cell size, while detectors placed at right angles or backward angles (e.g. RAS) respond mostly to granular features of cells. There is a continuum of detector response to cells from mostly size-related to mostly granularity-related as one moves through all angles from FSL to RAS.

Extinction requires a special explanation in AuRICA. The AuRICA optics focuses a semiconductor diode laser beam with a wavelength of 635 nm to a line that is much thinner than the diameter of a cell. When cells flow through this line focus, they block a certain amount of light, which is registered by the EXT detector. The moment that cell begins its travel across the line, focus is registered by the EXT detector, as is the moment that it ends its travel across the line focus. All cells move with very nearly the same velocity, therefore the time it takes for a cell to "fly" across the laser focus is proportional to the diameter of the cell. The parameter is referred to as "Time of Flight" or TOF. This is a new parameter that AuRICA uses to gate CD4 counts on lymphocytes and discriminate against monocytes.

In order to use this new parameter, it was essential that the AuRICA laser have very small random fluctuations in laser output power. This cannot be technically accomplished with argon lasers (fluctuations of one part in 50) but with a special engineering program the AuRICA diode laser fluctuations were lowered to one part in 10,000. Thus, both EXT and TOF became valuable new parameters.

The AuRICA light scatter parameters are used in the following way to classify cells. After red cell lysis, the three main classes of white cells are classified by a combination of FSH and TOF as shown in Figure 4. Lymphocytes, monocytes and granulocytes are shown as distinct clusters. This classification is the result of using the intrinsic properties of the cells without any labels.

Figure 4: Dot plot of TOF versus FSH, Showing Distinct Lymphocyte (Lower Left), Monocyte (Lower Right) and Granulocyte (Upper Right) Clusters

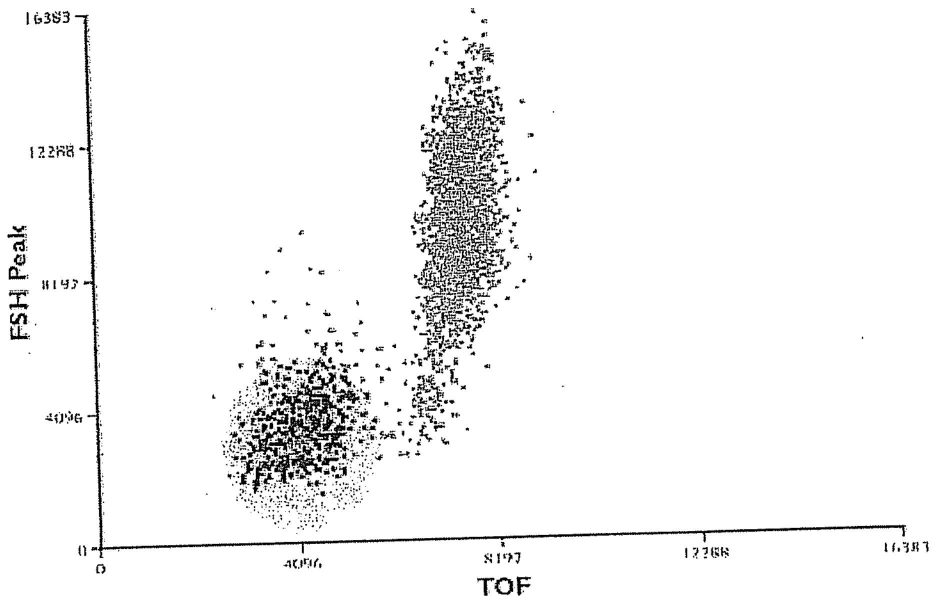


A few unlysed red cells appear directly above the lymphocytes. The total white cell count is obtained by summing the counts in the three white cell clusters while excluding counts in the region of unlysed red cells. The lymphocyte cluster shape is slightly variable from patient to patient, and owing to its importance in reporting CD4 and CD4%, the system uses an automatic cluster finding algorithm to adjust for any variability.

AuRICA uses a label to change the natural light scatter characteristics of the CD4 subclass of lymphocytes and perform CD4 counting. The label consists of anti-CD4 antibodies coupled to small gold particles. The particles are only slightly larger than an antibody which means that the conjugate forms a stable, colloidal suspension in liquid diluents where the particles never settle out of the suspension. When the particles bind to the surface of a cell, they add to the natural light scatter of the cell, but only in the directions that are sensitive to granularity. This means that the FSH versus TOF dot plot is unchanged when the gold conjugate binds to cell surfaces, but the light scatter signal at the RAS detector will change. Unbound colloidal gold does not affect the signal at any detector, which means that assays can be carried out without a "wash" step.

The AuRICA analytical software searches for the lymphocyte cluster in the FSH versus TOF dot plot and draws a gating region around the lymphocytes as shown in Figure 5.

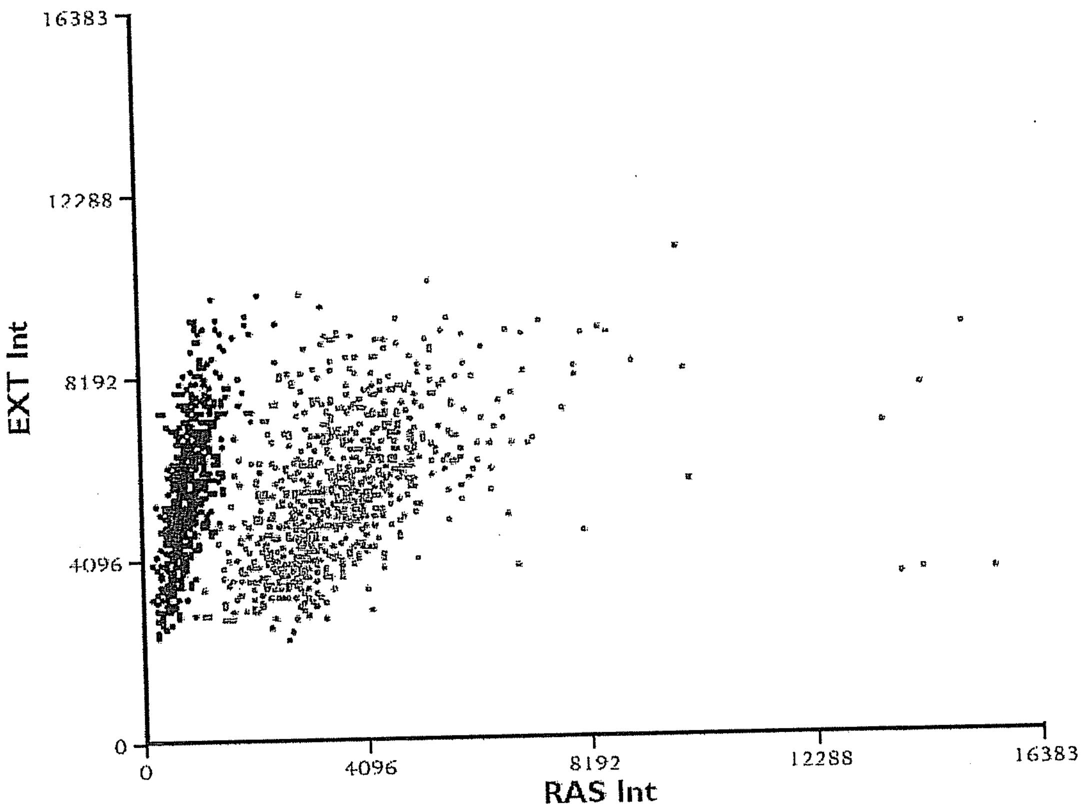
Figure 5: Dot Plot of TOF versus FSH Showing the Gating Region Around the Lymphocytes Which is Established by the Automatic Cluster Finding Software



Monocytes and red cells are excluded from the gating region. In cases where the exclusion is not sufficiently complete, the sample is "flagged," and the operator is warned by a message on the patient data summary.

Using this gate and displaying the lymphocytes on an EXT versus RAS dot plot (Figure 6), the lymphocyte cluster splits into two clusters. The left hand cluster contains all CD4 negative lymphocytes and the right hand cluster contains all CD4 positive lymphocytes. The AuRICA analytical software counts the cells in the right hand cluster and since the exact volume of blood is known, an absolute CD4 count can be reported.

Figure 6: Dot Plot of RAS versus EXT Showing How the Gated Lymphocytes From Figure 5 Become Resolved Into Two Distinct Clusters



On the left are CD4 negative lymphocytes, and on the right are CD4 positive lymphocytes. The cluster on the right gives the absolute CD4 lymphocyte count.

AuRICA reports the other white cell parameters differential counts from the FSH versus TOF dot plot.

Advantages of the Light Scatter Approach

The primary advantages of light scatter are as follows.

First, all light collection lenses are eliminated from the system as are all optical filters. This removes all of the sensitive optical elements of fluorescence flow cytometers that can become misaligned, and adds to the robustness of the instrument. This not only reduces cost by eliminating expensive lenses, filters, and high resolution mechanical adjustments and mounts, but also removes any need for optical alignment once the instrument leaves the factory. The AuRICA light scatter detectors and electronics are micro-fabricated and attached directly to the flow cell, which further reduces sources of misalignment.

Second, the colloidal gold light scatter reagents do not require refrigeration and do not need to be protected from the light. This is not the case for fluorescently labeled antibodies. The colloidal gold reagent is shipped in a capped tube in a dried state that resists damage by heat.

Third, AuRICA uses ordinary silicon photodiodes rather than photomultiplier tubes for optical detection. This reduces cost and system fragility significantly.

CD4SURE Reagents

CD4SURE reagents are supplied in prepackaged tubes that the operator loads into the system. These tubes contain the proper reagent dilutions and volumes, which makes it possible for the system to perform all pipetting steps automatically without any manual steps, or pre-run preparation. In order for AuRICA to be operated without any manual steps, the CD4SURE reagents must be factory dispensed in precise amounts. In order to eliminate the need for refrigeration of reagents, the ordinarily heat labile antibody markers are made heat stable through dessication. Therefore, the AuRICA system is classified as a "closed" system, in that only CD4SURE pre-packaged reagents will work to provide the advantages of eliminating manual steps, providing closed tube operation, and heat stable reagents.

CD4SURE reagents are designed to be shipped and stored without refrigeration. The only protein-based reagent is the colloidal gold antibody conjugate, which is dessicated to be temperature stable. The lyse reagent, the diluents, and the cleaning solution are in liquid form, and are inherently temperature stable for the dating period shown on the kit container, when stored at 20-25°C.

The conjugate is dessicated by a special process that differs from most methods. In many reagent dessication methods, the final reagent is dried onto the walls of the reagent tubes. In AuRICA, the volume of blood sample and diluent is only 50 μL which is too small to reconstitute a reagent that is on the tube walls. The CD4SURE gold conjugate is dried on a glass fiber pad that is centered at the bottom of the reagent tube. The sample and diluent are dispensed exactly over the position of the glass fiber pad, and solubilizes the conjugate. It takes approximately 2 seconds to dissolve the lyophilized conjugate.

Specialized reagents are used to clean AuRICA. One is the sheath, another is a dedicated cleaning reagent, and the last a specialized shutdown solution. In addition to a cleaning process that occurs for every sample, there is a shutdown cleaning process. Most of the AuRICA sample processing cycle is devoted to cleaning and self-maintenance. The shutdown cycle is completely devoted to

cleaning. This shutdown cycle takes place automatically after the operator loads a cleaning solution reagent tube and touches "Shutdown" on the screen. It does not require the operator be present during shutdown. An idle machine also executes a short cleaning cycle every few hours.

Outright clogs are avoided because the orifice on the probe that aspirates the sample and other liquids is smaller than any internal orifice. As a backup, the sample flow rate in the flow cell is electronically monitored every second. Any flow irregularities are analyzed, and if out of range, the sample is flagged when the results are reported on-screen and a cleaning cycle is prompted.

Internal Quality Control

There are several internal quality control check points in AuRICA, ranging from hardware checks to software checks.

Hardware Internal Quality Checks:

1. The system prevents the use of outdated reagents. All sample tubes and reagent tubes are barcoded and the barcodes are read inside the instrument. These barcodes contain reagent lot numbers and, most importantly expiration date information. If the system fails this internal quality check, the analysis process is stopped and the computer screen alerts the operator. The user has the option to carry on with analysis, with the expiration of the reagents appearing on the results screen printout.
2. The system prevents the aspiration or dispensing of the wrong reagent. The barcode reader also notifies the system that all tubes have been loaded into the proper positions and that the fluid handling probes have addressed the proper fluid. If the system fails this internal quality check, the analysis process is stopped and the computer screen alerts the operator, thus ensuring the reagents are used in the right order.
3. There is a quality check on the absolute volumetric fluid delivery. The sample flow rate is monitored every second during the analysis phase of the instrument cycle. Deviations from an accepted time profile of the flow rate curve are analyzed and flagged if unacceptable. This quality check is used to assure that the absolute volumetric fluid delivery of the on-board syringe pumps is repeated on each sample.
4. The position of the aspiration and dispensing probes is monitored by the system, as an internal check that the proper reagent is aspirated or dispensed.
5. The aspiration and dispensing probes are electronically monitored to check their position in or above the fluid level in the tubes. This prevents the tips from being submerged by more than a fraction of a millimeter,

and also assures that they are "tipped off" when dispensing small volumes.

6. The flow rate monitor also reports the passage of non-cellular particulates in order to alert the operator to possible malfunctions in the automatic cleaning processes.
7. The internal barcode system keeps track of patient identification and prevents the inadvertent running of the same patient twice while nevertheless allowing deliberate re-runs

Analytical Software Internal Quality Checks:
The AuRICA system employs automated analytical software. This means that the analytical software locates all dot plot clusters, sets gates, and sets counting regions without operator participation. In fact, the operator cannot view the dot plots.

The quality of flow cytometry and hematology dot plots is affected by the disease state of the patient, the physical condition of the sample and the condition of the instrument and its reagents. The analytical software in AuRICA was designed for clinics where a skilled supervisor is not available to judge the quality of a dot plot. The system substitutes for the supervisor by searching for a number of features that rate the quality of the dot plot and "flags" those that do not meet certain internal quality standards. In some cases only certain parameters are affected by a lower quality dot plot, and these are not reported for that patient. In other cases all parameters are affected and therefore not reported.

Dot plot clusters are rated by their being well-defined, being positioned within expected limits, having shapes within accepted limits, having counts within accepted limits, and being free of encroachment from other clusters. Clusters are accepted for analysis if they meet an internal quality rating standard. In general, these standards are conservative, and follow the design philosophy that it is best to flag a suspicious result even though it may have been a correct result, and recommend reanalysis. Consequently the "flag rate" of a AuRICA system may be higher than the flag rate for manually operated flow cytometers where a skilled supervisor is available. The recently developed CD4SURE lysing system has reduced the flag rate in hard to lyse samples significantly over gentler ammonium chloride based lysing. Antigen presentation is excellent with the improved lyse reagent.

External Quality Control
The emphasis of external quality control has evolved over time as systems have become more automated, and manual steps such as daily reagent make-up,

pipetting, mixing, and incubation of samples have become out-of-date. When systems required complex manual steps, the emphasis of external quality control was to check the proficiency of the operator. With fully automated systems, the emphasis has become to check the condition of the system.
Commercial suppliers have created control materials that carry labeled assay values and ranges for hematology and cell surface marker assays. AuRICA uses two distinct commercial quality control materials; one for hematology parameters and one for CD4 parameters. Samples of control materials are run like patient samples. The results screens are modified to show what control levels were run, the result, and the expected result range. The user's manual lists the accepted commercial external quality control products. The New CD4SURE reagent system has significantly expanded the list of accepted external quality control materials.

Automatic Preventive Maintenance
Those that are familiar with flow cytometry will immediately appreciate the need to maintain clean fluid lines. The AuRICA provides this automatically.

Outright blockages by clots in the blood sample are prevented by virtue of the fact that the aspiration probe has a smaller orifice cross section than any subsequent orifice in the system.

The rest of the preventive maintenance consists of timely automatic flushing cycles. For example, after every ten samples, the system prompts the operator to touch "Clean" on the computer screen. The system then takes a brief "time out" to execute an internal wash. If the system has not run a sample for two hours or more, an automatic maintenance cycle runs for approximately 30 seconds. At the end of the day, the operator replaces the waste bottle with a shutdown solution and loads a capped, cleaning solution tube in position 4 of the tube rack. The operator touches "Shutdown" on the computer screen and can at that point leave the system until the next shift starts. During the 1 hour and 20 minute automatic shutdown cycle, the system is thoroughly washed and made ready for the next round of samples. During the night or other "off hours" following shutdown, the system automatically executes a prime cycle every hour to maintain wetted lines until it is called upon for further use. If the system has not been shut down properly, the system performs some level of self-cleaning every hour, but the next shift operator is warned on the computer screen, and is forced to execute the shut down cycle and a prime cycle before samples can be processed.

These automated fluid care steps are needed for the long term reliability of any flow cytometer. The AuRICA system is designed to provide this reliability through automation and not through operator training.

CONCLUDING REMARKS

This system overview has emphasized the CD4 and related parameter capabilities of AuRICA. As such, the AuRICA system can be expected to shift the first line of defense for many diseases away from central laboratories and into decentralized clinics that will, in the future, deliver a high level of medical care.

In the beginning, there were only questions.
Thanks to the following friends and colleagues,
we were able to find the answers.

Republic of Botswana
Dr. Gabriel Anabwani
Dr. Iqbal Chand
Waheeda Chand
Dr. Mark Kline
Rachel N. Khama
Dr. Ali Kombe
Leonard Manthe
Dr. D. O. Mompati
Dr. K. F. Mompati
Dr. Trevor Peter

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Nathan Geffen
Dr. Debbie Glencross
Ashraf Grimwood
Dr. Dave Johnson
Dr. Des Martin
Dr. Steven Miller
Dr. Nhlanhla Msomi
Dr. Lesley Scott
Dr. Ronin Wood

Canada
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United Republic of Tanzania
Kenneth Lema
Dr. Meshak Massi
Grace Mbekm
Prof. Fred Mhalu
Dr. Willy Urassa

Barbados
Dr. Akin Abayomi
Songee Branch
Dr. Clive Landis

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Osi Peter Asika

United States of America
Harold Flynn
Dr. Edmund Kowaloff
John Roche
Dr. Howard Shapiro
Dr. Thomas Spira
Bonnie Jenson

For more information, please contact your local PointCare Technologies representative, or visit www.pointcare.net

EXHIBIT B

HMA PBK

PRODUCT SPECIFICATIONS FOR HT INSTRUMENT

CR-008-015	Plt reportable range from 10-2000 K/uL	PR-008-015	Large dynamic range for Plt with CV% at 250K/uL < 3%	Desirable ϕ1 Mandatory ϕ2
CR-008-016	MPV reportable range from 2-25 fl	PR-008-016	Large dynamic range for MPV with CV% at 10 fl < 5%	Desirable ϕ1 Mandatory ϕ2
CR-008-017	32 hour sample age for CD4 and CD4%. 8 hours for all other parameters.	PR-008-017	Sample age extension for CD4 and CD4% from 8 hour age requirement	Desirable ϕ1 Mandatory ϕ2
CR-008-018	System warns user if results possibly compromised by aged sample.	PR-008-018	Mitigation factors for sample age, such as data entry for draw time, flagging for scatter plots, and training	Mandatory ϕ1
CR-008-019	System does not report results if compromised by aged sample.	PR-008-019	Absolute internal control for sample age	Desirable ϕ1
CR-008-020	Minimum of 100 samples (including controls) in 7.5 hours	PR-008-020	4.5 minutes per sample	Mandatory ϕ1
CR-008-021	Instrument may operate for minimum of 1 hour or 30 samples unattended	PR-008-021	Cap piercing autoloader capable of processing up to 30 samples	Desirable ϕ1
CR-008-022	Autoloader capable of handling standard tube sizes	PR-008-022a	Currently standard 5mL size tubes can be used	Mandatory ϕ1
		PR-008-022b	Expand possibilities to other sizes for future development	Desirable ϕ2
CR-008-023	Choice of CBC/CD4 or CBC only	PR-008-023	Choice of sequence from menu or separate worklist. Barcode could be design to determine which sequence to be used	Mandatory ϕ1
CR-008-024	Minimum 5-pt WBC differential with CD4	PR-008-024	Two passes through flow cytometer—WBC differential without immunogold and CD4% with immunogold. Lym count to be determined either by impedance or optical without gold.	Mandatory ϕ1
CR-008-025	Minimal sample volume used in assay	PR-008-025a	180 uL for CBC and an additional 45 uL for CD4	Mandatory ϕ1
		PR-008-025b	Minimum 1.5mL sample volume supplied	Mandatory ϕ1
CR-008-026	No handling of open blood tubes	PR-008-026	Automated cap piercing blood sampling (with autoloader)	Mandatory ϕ1
CR-008-027	Touch screen computer operation	PR-008-027	Touch screen computer specified	Mandatory ϕ1
CR-008-028	Mitigation of computer theft	PR-008-028	Option for security cable for computer	Mandatory ϕ1
CR-008-029	Printable results in black and white	PR-008-029a	B&W printer specified	Mandatory ϕ1
		PR-008-029b	Color printer specified	Optional ϕ1
CR-008-030	Local languages available for each market	PR-008-030	English, French, Portuguese, Spanish, Chinese, Thai, Vietnamese, and Russian screens	Desirable ϕ1 Mandatory ϕ2

R3

EXHIBIT C

From: Don Barry
Sent: 3/16/2007 8:08:34 PM
To: Gary Young
CC:
Subject: RE:

Hi Gary,

I feel bad and somewhat responsible that we are having trouble with that optical sensor. I know that you guys sent me some Lexan to test with and I had said that it would be ok. This reagent is very difficult to deal with and we have been stumped and have had three or four other engineering groups stumped at finding materials that can be machined and are compatible. I know that the small channels of the gold channel are virtually impossible to polish and this is may be the cause of the buildup. It may be possible to switch to Delrin, which seems to work well with the gold reservoir, if an infrared sensor can read through it.

The rest of the design of the instrument is quite impressive. Before our issue yesterday, I saw some of the best CD4 clusters ever on any instrument that we have worked at PointCare, including our current platform. It was difficult for me to get any work done for the first day that we had the instrument installed because everyone kept bothering me to show them the dotplots! The lysing step was almost at a point where the cycle is complete. I was actually surprised to see that you guys got that far. It is such a difficult reagent system to work with that I spent nearly 4 months to get it to work on our current platform, which included a week of work with the guy who led the team that development the reagents.

We are real close to getting this system finalized and I just need the help of your team to get these last few pieces tweaked.

Thanks,

Don

From: Don Barry

DEPOSITION EXHIBIT
PENGAD 800-631-6989
Barry 4
3-27-08

Sent: Friday, March 16, 2007 2:40 PM
To: 'Gary Young'
Subject: RE:

Hi Gary,

Nobody will be at PointCare tomorrow, so Saturday delivery will not be necessary. I was thinking of coming in, but we are getting hit with a blizzard tonight. I would like to get started on Monday morning, if possible.

Did you decide on trying a glass tube for the gold measurement? I am very concerned that even if we replace the board, we will still have an issue with the gold build-up in the channel with the current design. Did you guys come up with a different solution?

Thanks,

Don

From: Gary Young [mailto:gyoung@mwi-danam.com]
Sent: Thursday, March 15, 2007 4:53 PM
To: Don Barry
Subject: RE:

Don,

The board and sensors will not ship today. We will ship them tomorrow with overnight delivery.

Gary

From: Don Barry [mailto:debarry@pointcare.net]
Sent: Thursday, March 15, 2007 3:41 PM
To: Gary Young
Subject:

Hi Gary,

Does it look like you will be able to ship another board and sensors today?

Thanks,

Don